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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,966	01/12/2004	John Paul Helgeson	WARF-0235	3588

23377 7590 09/28/2006

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EXAMINER	
IBRAHIM, MEDINA AHMED	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/755,966	HELGESON ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *33-37 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10,12-15,17-32,38-40,42-45 and 47-65* is/are rejected.

7)☐ Claim(s) *4,11,16 and 41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-32, 38-45, and 47-65 in the reply filed on 08/22/06 is acknowledged. Applicant is reminded that the restriction requirement between the nucleic acid sequences is not based upon election of species because each nucleic acid is not a member of single genus invention, but constitutes an independent and patentably distinct invention. Nucleotide sequences encoding different proteins are structurally distinct chemical compounds that are unrelated to one another, as are different proteins are structurally distinct chemical compounds that are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Each sequence requires an independent search of the sequence databases. Examiner, however, notes that SEQ ID NO: 7 and 4 can be examined together, since SEQ ID NO: 4 is a mutant form of SEQ ID NO: 7. Therefore, SEQ ID NO: 4 and 7 are hereby rejoined. The restriction requirement is made FINAL.

Claims 1-65 are pending.

Claims 33-37, and 46 are withdrawn from consideration as being directed to the non-elected invention.

Claims 1-32, 38-45, and 47-65 are examined.

Copending Application

Applicant must bring to the attention of the Examiner of a particular application, information with their knowledge as to other copending United States applications,

which are "material to patentability" of the applications in question. MPEP 2001.06(b). See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CAFC 2003).

Specification

The application has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The disclosure is objected to because of the following informalities: for example, page 1, line 25, contains embedded hyperlinks directed to an Internet address. The use of hyperlinks and/or other form of browser- executable code are not permitted under USPTO current policy because the content of such links are subject to a change, resulting in the introduction of New Matter into the specification. Applicant is required to delete all embedded hyperlinks and/or other forms of browser- executable code. See MPEP 608.01.

Claim Objections

At claims 40-41, "at" is deleted, for clarification.

At claim 45, "a phenotype associated with" is deleted for clarification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. The claim is indefinite because what is encompassed by "labeled" polynucleotide is unclear and is not defined in the specification. Therefore, the metes and bounds of the claim are unclear. Clarification is required to more clearly define the metes and bounds of the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-10, 12-15, 17-32, 38-40, 42-45, and 47-65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding SEQ ID NO: 8, a recombinant expression cassette comprising it, a host cell/plant transformed with said nucleic acid, and a method of transforming a plant with said nucleic acid, does not reasonably provide enablement for sequences having at least 70% or 95% identity to the disclosed sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to an isolated nucleic acid comprising a polynucleotide having at least 70% or 95% identical to SEQ ID NO: 4 or 7 or sequence that hybridize thereof under stringent conditions, said polynucleotide encoding a polypeptide that confers disease resistance upon expression in a plant, and

polynucleotides encoding a polypeptide having at least 70% identical to SEQ ID NO: 8 and that confers disease resistance upon expression in a plant. The claims are also drawn to a recombinant expression vectors comprising said nucleic acids, plants transformed with said nucleic acids, and methods for transforming plants with said nucleic acids for disease resistance. The claims are further drawn to DNA fragment/segments of an RB gene including genes with a coding region having at least 70% identity to SEQ ID NO: 7 or 4 and sequences hybridizing thereto under stringent conditions, said DNA fragments/ segments capable of controlling/modulating expression of an operably linked coding region in a transgenic plant.

Applicant teaches isolation and identification of an RB resistance gene and resistance gene homologs from *Solanum bulbocastanum*, said gene having a coding region identified as SEQ ID NO: 7 encoding an NBS-LRR protein type, and with a promoter region identified as SEQ ID NO: 23. Applicant also teaches transformation of potato with SEQ ID NO: 7, and methods for screening transgenic potato plants expressing SEQ ID NO: 7 for resistance against Phytophthora infestans. Applicant provides amino /nucleic acid comparison between the coding regions from disease resistance and susceptible potato variety, and comparison of the RB resistance protein with resistance homolog proteins of RGA1, RGA3, RGA4 (Examples 1-6 and 8). Applicant also teaches that SEQ ID NO: 4 is a mutant coding region of RB, but no function as a result of the mutagenesis has been disclosed.

Applicant has not provided guidance for how to identify or obtain all the nucleic acids having both the structural and functional limitations as recited in the claims. The

breadth of the claims encompasses sequences obtainable by modifications including multiple deletions and/or substitutions of nucleotide/amino acids in SEQ ID NO: 4, 5, 7 or 8. However, Applicant has not taught which regions in SEQ ID NO: 4, 5, 7 or 8 that would tolerate such modifications. Applicant has not taught a single variant having both the structural and functional property as recited in the claims. Applicant has not provided guidance for modifications to SEQ ID NO: 7 or 4 that resulted nucleotide sequences of claims 1-2 and 10. Claims drawn to SEQ ID NO: 4 are included in the rejection because the specification merely refers SEQ ID NO: 4 as a mutant coding sequence, however, the specification does not teach that a mutant RB coding sequence can also provide disease resistance activity. Also, antisense and complementary sequences of SEQ ID NO: 7 are not expected to provide disease resistance activity.

While mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims. One skilled in the art would expect any tolerance to modification for a given DNA/protein to diminish with each further and additional modification or multiple substitutions/ deletions. One skilled in the art would have to make all possible nucleotide/amino acid substitutions and deletions in the 3kb or the 970 long disclosed sequences and test all nucleic acid/polypeptide sequences that meet the structural limitations to determine which would also meet the functional limitation. In the absence of specific guidance as to how and where to modify the disclosed sequences, undue experimentation would be required to screen through the myriad of different nucleic acids having 70% and 95% identity to SEQ ID NO: 4 or 7 or hybridizing sequences thereof and polypeptides having

at least 75% identity to SEQ ID NO: 8, to determine which nucleic acids/polypeptides are capable of providing disease resistance upon expression in a transgenic plant.

Osumi et al (US 20040237137 A1, Published 25/11/04) teach isolated homologous resistance genes encoding proteins having at least 93% amino acid sequence identity to a known disease resistance protein but are non-functional disease resistance proteins (see at least paragraphs 0072-0073; and Figure 5).

Furthermore, since the working example disclosed in the specification is limited to the use of the unmodified nucleic acids encoding SEQ ID NO: 8, the ability of said nucleic acids to encode a functional polypeptide that confers resistance against *Phytophthora infestans* cannot be extrapolated to all the nucleic acids as broadly claimed, absent specific guidance. Therefore, when In re Wands factors are weighed it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims, and therefore the invention is not enabled.

Claims 51-65 are further rejected because the specification is not enabling promoter sequences other than the promoter sequence of SEQ ID NO: 23. Applicant has not provided guidance for the specific isolation of all promoter and terminator sequences from all RB genes. The state of the art for isolation of genomic clones with specific function is highly unpredictable. Significant guidance is required with respect to hybridization and wash (or PCR) conditions; probe (or primer) sequences that will allow specific isolation of the target genes from various plant sources. In the absence of

specific guidance, undue trial and error experimentation would be required to screen through the vast number of genomic clones to identify target genes that contain the desired promoter and/or polyadenylation signal. Undue experimentation would also be required to screen through the myriad of different DNA segments comprising different 5' and polyadenylation regions of said target genes and variants thereof, to determine which DNA segments would have promoter activity including pathogen responsive promoter activity, and which DNA segments are capable of modulating of an operably linked coding sequence upon expression in a transgenic plant.

The state of the prior art, as evidenced by Kim et al (Plant Molecular Biology, vol. 24, pp. 105-117, 1994) teaches unpredictability inherent in the identification and function of promoters. Kim et al. teach the extreme sensitivity of promoter regions to single base pair changes, the absolute requirement for as few as 3 to 6 nucleotides for promoter function, and the failure of a promoter to function either constitutively or specifically when lacking oligonucleotide regions approximately 100 bp upstream of the transcription start site (page 106, paragraph bridging the columns; paragraph bridging pages 107 and 108; page 110, paragraph bridging the columns). Therefore, given the breadth of the claims; the lack of guidance; the unpredictability inherent in promoter functionality; the limited working examples; and the state of the art, as discussed supra, the claimed invention is not enabled throughout the broad scope. See *Amgen Inc. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1021 and 1027 (Fed. Cir. 1991) at page 1021, where it is taught that a gene or a promoter is not reduced to practice until the inventor can define it by its "physical or chemical properties" (e.g. a DNA

sequence) and page 1027, where it is taught that the disclosure of a few gene sequences did not enable claims broadly drawn to any analog thereof.

Written Description

Claims 1-2, 5-10, 12-14, 17-32, 38-39, 42-45, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to isolated nucleic acids having at least 70% or 95% identical to SEQ ID NO: 4 or 7, sequences that hybridize thereof under stringent conditions, said polynucleotides encoding polypeptides that confers disease resistance upon expression in a plant, and polynucleotides encoding a polypeptide having at least 70% identical to SEQ ID NO: 8 and that confers disease resistance upon expression in a plant. The claims are also drawn to DNA segments comprising promoter and polyadenylation signal from any RB gene and from the nucleic acids above. The claims are also drawn to a recombinant expression cassettes comprising said nucleic acids, plants transformed with said plants, and methods for transforming plants with said nucleic acids for resistance against *Phytophthora infestans*. In contrast, Applicant describes nucleic acids encoding SEQ ID NO: 8, and the promoter sequence of SEQ ID NO: 23, expression cassettes comprising said nucleic acids, and transgenic plants, and methods of transforming plants with said nucleic acids. These are genus claims.

In *Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), the court stated:

An adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties", not a mere wish or plan for obtaining the claimed chemical invention... Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself (43 USPQ2d at 1404).

The court held that held that human insulin-encoding cDNA is not described by prophetic example, which sets forth only a general method for obtaining the human cDNA:

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity...Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes...does not necessarily describe the DNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA....Accordingly, the specification does not provide a written description of human cDNA (43 USPQ2d at 1405).

The description of a single species of rat cDNA was held insufficient to describe the broad genera of vertebrate or mammalian insulin:

"In claims to genetic material...a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It doesn't define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is (43 USPQ2d at 1406).

The court continued:

"Thus...a cDNA is not defined by the mere name 'cDNA', even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". (43 USPQ2d at 1406). See, also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to

provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Applicant has not described the composition or structure of all the nucleic acids, DNA segments comprising promoters and polyadenylation signal as broadly claimed. A substantial variation in structures and function is expected among nucleic acids from any plant source having 70% sequence identity to SEQ ID NO: 4 or 7, and nucleic acids encoding polypeptides having at least 70% identity to SEQ ID NO: 8. Applicant has not described the composition or structure of a DNA segment commencing at a location about 2500 bases upstream from a transcription initiation site and ending at a location about 250 bases downstream from the transcription initiation site of an RB gene, and fragments of said DNA segments. Therefore, Applicant has not described a representative number of nucleic acids encoding RB polypeptides and a representative number of DNA segments comprising promoter and polyadenylation signal, of the genus of the claims. In addition, since Applicants has not described the nucleic acids/DNA segments of the claims as discussed above, expression cassettes, cells and plants cell comprising said nucleic acids, and methods that employ said nucleic acids/promoter/DNA segments are similarly not described. See Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

Remarks

The Claims are deemed free of the prior art of record.

Claims 4, 11, 16, and 41 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and if the objection to the claim as set forth above is obviated.

No claim is allowed.

Contact information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

9/7/06
Mai

MEDINA A. IBRAHIM
PRIMARY EXAMINER